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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,266	03/05/2001	Robert L. Bratzler	C1037/7017 (HCL/MAT)	3753

23628 7590 08/28/2002

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EXAMINER
ANGELL, JON E

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/800,266	Applicant(s) BRATZLER ET AL.	
	Examiner J. Eric Angell	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,21,31 and 36* is/are pending in the application.

4a) Of the above claim(s) *21 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-17, 21, 31 and 36 are pending in the application.

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-17 and 31) and of the species: Paxex/Paxlitaxel, Herceptin, Her2/neu, and estrogens in Paper No. 9 filed June 5, 2002 is acknowledged. The traversal is on the ground(s) that search and examination would not require an undue search burden. This is not found persuasive because each Group is drawn to subject matter of different classification, as set forth in the previous Office Action. Different classification is prima facie evidence of a search burden to search the different Groups.

The requirement is still deemed proper and is therefore made FINAL.

Claims 21 and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9, filed June 5, 2002.

The examiner would like to thank Applicants for pointing out the typographical error in the previous action. Group I should consist of claims 1-17 and 31, as pointed out by the Applicants. Claims 1-17 and 31 are examined here in.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-17 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states on page 1404:

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to a method for treating a subject having, or at risk of developing a cancer, comprising administering an immunostimulatory nucleic acid and a cancer medicament in an amount sufficient to treat cancer or reduce the risk of developing cancer. Therefore the nature of the invention is in the field of cancer treatment, and encompasses immunotherapy as the methods are drawn to administration of an immunostimulatory nucleic acid.

The breadth of the claims

The breadth of the claims is very broad. For instance, the broadest embodiment of the invention encompasses administering any poly-G nucleic acid (regardless of size) and any cancer medicament to treat or prevent any type of cancer in any species of animal, including humans.

The unpredictability of the art and the state of the prior art

The relevant art teaches that immunotherapy of cancer is unpredictable. For instance, regarding the unpredictability of immunotherapy of cancer, Gouttefangeas et al. (Nature Biotechnology Vol. 18:491-492; 2000) teaches, "effective immunotherapy has remained elusive because of three major problems: first, for many tumors, no or not enough suitable antigens are known; second, no consensus exists for the best antigen formulations or the rout of immunization; and third, tumors under immune attack tend to be selected for antigen loss variants." (See p. 491, first paragraph). Specifically regarding the immunostimulatory effects of oligodeoxynucleotides, Gouttefangeas points out, "we do not yet know whether such constructs [immunostimulatory oligonucleotides] work in humans. Some immunostimulatory effects of CpG motifs have been described in human peripheral blood in vitro, most notably in dendritic cells, but immunization trials have not been reported. Thus, the efficacy of CpG-protein constructs for immunotherapy in patients remains to be tested." (See p. 492, middle column, first paragraph).

Old (Scientific American, 9/96, cited in IDS) also recognizes several problems that render cancer immunotherapy unpredictable. For instance, Old teaches, "Despite the great hope of immunotherapy, a dark cloud hangs over all our attempts to control cancer by immune mechanisms. Caner cells are masters of deceit and disguise-veritable Houdinis that can readily

alter themselves to evade immunological recognition and attack." (See p. 11, under "The hurdles ahead"). Furthermore, Old teaches, "[I]t is conceivable that cancer vaccines may injure normal cells to some degree" and points out, "There are a number of disease states, called autoimmune diseases, that arise when the immune system turns against normal tissues in the body." (See p. 11, under "The hurdles ahead"). Finally, Old teaches, "[W]e need to exert considerable caution in making any predictions" clearly indicating the unpredictable nature of immunotherapy (See p. 11, under "The hurdles ahead").

The relevant art recognizes several significant and unpredictable obstacles that must be overcome for immunotherapy. The instant application does not offer any evidence that the claimed invention has overcome any of these recognized obstacles.

To overcome the teachings in the art, the specification would need to supply direct, correlative guidance on how to administer the therapeutic composition to a subject in such a way that the treatment consistently, effectively, and predictably treats every type of cancer.

Working Examples and Guidance in the Specification

The specification has no working examples, whatsoever, of effective treatment of any type of cancer using the claimed composition. The specification does disclose a variety of precise protocols for the administration of the composition. However, no data is presented supporting the notion that the claimed invention is an effective cancer treatment. Nor does the specification disclose any working examples or guidance which overcome the unpredictability of cancer therapy, as recognized in the art. Furthermore, no guidance is provided as to the dosage amount or frequency required to effectively treat cancer. It would essentially be a trial and error

process to make and use the diverse species of therapeutic molecules encompassed by the claims. Therefore, without any supporting data, it is not predictable that the claimed treatment method would effectively achieve any therapeutic benefit.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since determination of the efficacy of the claimed treatment would require, initially, animal testing to determine the efficacy of every therapeutic composition on every possible type of tumor in animal models, showings not present in the specification. After successful experimentation in test animal, the efficacy of the treatment would have to be tested in human subjects, an unpredictable and difficult undertaking in itself. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the high degree of unpredictability of immunotherapy and cancer treatment recognized in the art, the breadth of the claims, the lack of working examples and guidance in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed method is undue.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
August 15, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER